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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/843,007	04/26/2001	Jens Kossmann	GFB-I DIV1	9893

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EXAMINER

BAUM, STUART F

ART UNIT	PAPER NUMBER
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1638

DATE MAILED: 10/23/2002

9

Please find below and/or attached an Office communication concerning this application or proceeding.

**Office Action Summary**

Application No.

09/843,007

Applicant(s)

KOSSMANN ET AL.

Examiner

Stuart F. Baum

Art Unit

1638

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

- 1) ☒ Responsive to communication(s) filed on 02 August 2002.
- 2a) ☐ This action is **FINAL**.                      2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

- 4) ☒ Claim(s) 2,8 and 19-46 is/are pending in the application.
- 4a) Of the above claim(s) 2,8,19-32,39 and 42-46 is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 33-38,40 and 41 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

**Application Papers**

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 02 August 2002 is/are: a) ☐ accepted or b) ☒ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on \_\_\_\_\_ is: a) ☐ approved b) ☐ disapproved by the Examiner.
- If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

**Priority under 35 U.S.C. §§ 119 and 120**

- 13) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All   b) ☐ Some \*   c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- \* See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
- a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

**Attachment(s)**

- 1) ☒ Notice of References Cited (PTO-892)                      4) ☐ Interview Summary (PTO-413) Paper No(s). \_\_\_\_\_
- 2) ☒ Notice of Draftsperson's Patent Drawing Review (PTO-948)                      5) ☐ Notice of Informal Patent Application (PTO-152)
- 3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) \_\_\_\_\_                      6) ☐ Other: \_\_\_\_\_

Art Unit: 1638

### **DETAILED ACTION**

1. Applicant's election without traverse of Group V, claims 20, 21, 33-38, and 40-41 in Paper No. 8 is acknowledged.

2. Claims 2, 8, and 19-46 are pending.

Claims 20 and 21 have been amended.

Claims 2, 8, 19, 22-32, 39, 42-46 are withdrawn from consideration because they are drawn to non-elected subject matter.

Claims 20 and 21 are withdrawn from consideration because the body of the claim is drawn to non-elected material, Group VI, even though the preamble is directed to the elected invention.

Claims 33-38 and 40-41 will be examined on their merits.

### ***Claim Objections***

3. Claims 33, 35 and 40 are objected to for depending on a non-elected claim.

### ***Drawings***

4. The drawings are objected to for the reasons indicated on the enclosed form PTO-948. Correction is required.

***Claim Rejections - 35 USC § 112***

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

5. Claims 36, 37, and 38 and all subsequent dependent claims are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

In claim 36, the article “an” preceding “apoplast” should be changed to --the--.

In claim 37, the article “a” preceding “apoplast” should be changed to --the--.

In claim 37, --claim 35-- should be inserted before “(ii)”.

In claim 38, --claim 35-- should be inserted before “(i)”.

Claim 38 is indefinite and unclear in the recitation “sucrose storage organs of the plant”. Applicant has not defined this term nor has Applicant pointed out which organs of a plant store sucrose nor has Applicant pointed out which plants possess “sucrose storage organs”. The common storage compound in plants is starch.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

6. Claims 33-38 and 40-41 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The claims are drawn to a process for the production of linear  $\alpha$ -1,4 glucans, fructose and/or fructose syrup comprising culturing a host cell or microorganism, wherein the host cell or microorganism secretes amylosucrase into a culture medium comprising sucrose and recovering the produced  $\alpha$ -1,4 glucans and/or fructose, a process for the production of linear  $\alpha$ -1,4 glucans in plants comprising transforming a plant with an expression cassette comprising a promoter operably linked to an amylosucrase enzyme wherein in one embodiment the enzyme is directed to either the vacuole or apoplast and in another embodiment the enzyme is not directed to the vacuole or apoplast, and lastly the Applicants claim a process for the production of linear  $\alpha$ -1,4 glucans, fructose and/or fructose syrup in vitro comprising incubating an amylosucrase enzyme in a sucrose solution and recovering the produced  $\alpha$ -1,4 glucans and/or fructose from the solution.

The Applicants disclose the isolation of a genomic sequence encoding an amylosucrase from *Neisseria polysaccharea* which was subcloned into the vector pNB2 and transformed into *E. coli*. Amylosucrase was detected both within *E. coli* and in the medium in which the *E. coli* were grown. The Applicants do not identify structural features unique to the *N. polysaccharea* amylosucrase protein, the functional domains of the protein nor the overall function of the protein. The Federal Circuit has recently clarified the application of the written description requirement to inventions in the field of biotechnology. See University of California v. Eli Lilly and Co., 119 F.3d 1559, 1568, 43 USPQ2d 1398, 1406 (Fed. Cir. 1997). In summary, the court stated that a written description of an invention requires a precise definition, one that defines the structural features of the chemical genus that distinguishes it from other chemical structures. A definition by function does not suffice to define the genus because it is only an indication of

Art Unit: 1638

what the gene does, rather than what it is. Given the lack of description for the *N. polysaccharea* amylosucrase protein, it remains unclear what features identify a *N. polysaccharea* amylosucrase protein or a protein exhibiting amylosucrase activity given the lack of an assay to identify proteins with a clear amylosucrase activity. Since a *N. polysaccharea* amylosucrase protein has not been described by specific structural features or by specific function, the specification fails to provide an adequate written description to support the generic claims.

7. Claims 33-38 and 40-41 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The claims are drawn to a process for the production of linear  $\alpha$ -1,4 glucans, fructose and/or fructose syrup comprising culturing a host cell or microorganism, wherein the host cell or microorganism secretes amylosucrase into a culture medium comprising sucrose and recovering the produced  $\alpha$ -1,4 glucans and/or fructose, a process for the production of linear  $\alpha$ -1,4 glucans in plants comprising transforming a plant with an expression cassette comprising a promoter operably linked to a amylosucrase enzyme wherein in one embodiment the enzyme is directed to either the vacuole or apoplast and in another embodiment the enzyme is not directed to the vacuole or apoplast, and lastly the Applicants claim a process for the production of linear  $\alpha$ -1,4 glucans, fructose and/or fructose syrup in vitro comprising incubating an amylosucrase enzyme in a sucrose solution and recovering the produced  $\alpha$ -1,4 glucans and/or fructose from the solution.

The Applicants do not reduce to practice their invention. They only disclose the isolation of a genomic sequence encoding an amylosucrase from *Neisseria polysaccharea* which was subcloned into the vector pNB2 and transformed into *E. coli*. Amylosucrase was detected both within *E. coli* and in the medium in which the *E. coli* were grown. Both soluble and insoluble products were detected in the growth medium but Applicants do not disclose the identity of the products. The Applicants have not demonstrated that  $\alpha$ -1,4 glucans, fructose and/or fructose syrup can be produced and isolated from: a culture medium comprising bacteria expressing a amylosucrase, a plant transformed with an amylosucrase, or a solution comprising an isolated amylosucrase enzyme including the sucrose substrate.

Producing  $\alpha$ -1,4 glucans using amylosucrase does not always produce the expected results. Applicant's own admitted statement that products, other than the desired  $\alpha$ -1,4 glucans were produced even in their system (page 36, lines 3-12). Remaud-Simeon et al (1995, Carbohydrate bioengineering. Proceedings of an International Conference, Elsinore, Denmark. Pages 313-320. Vol 10 in the series, Progress in Biotechnology) teach that concentrations of sucrose higher than 30 g/l inhibit the amylosucrase and the enzyme is not only activated by sucrose but also by glycogen, starch and maltooligosaccharides (page 319, 2<sup>nd</sup> paragraph). Remaud-Simeon et al conclude that the enzyme is activated by glycogen, starch and maltooligosaccharides and can catalyze other reactions (abstract). de Montalk et al (2000, FEMS Microbiology Letters 186(1)103-108) teach that glycogen is an activator of amylosucrase and that this interaction is sucrose concentration dependent (page 106, 1<sup>st</sup> paragraph of Discussion). De Montalk points out that sucrose and glycogen both bind to the enzyme (page 106, 1<sup>st</sup> paragraph of Discussion and page 107, 3<sup>rd</sup> paragraph), and that the enzyme has binding sites for

Art Unit: 1638

other carbohydrates, not just sucrose (abstract). de Montalk et al (2000, FEBS Letters 471 (2/3):219-223) teach that amylosucrase synthesizes a large diversity of products in the presence of sucrose as a sole substrate and that the enzyme is capable of several different reactions in a non-Michaelian kinetic behaviour (page 223, Conclusion paragraph). Albenne et al (2002, FEBS Letters 527(1-3):67-70) teach that amylosucrase from *Neisseria polysaccharea* can catalyze reactions other than the cleavage of the alpha 1-beta 2 linkage of sucrose (page 70, 1<sup>st</sup> paragraph).

The Applicants have claimed a process for the production of  $\alpha$ -1,4 glucans in plants but they have not specified which plants, or in what organs the  $\alpha$ -1,4 glucans will be made. Most plants do not store sucrose but rather, the storage compound for plants is starch. Given that the Applicants' invention calls for sucrose to be used as a substrate for amylosucrase, it is not clear how the  $\alpha$ -1,4 glucan product will be made given the lack of storage sucrose. Sucrose is transported in the phloem but Applicants have not disclosed a method of utilizing phloem sucrose in their invention. Also, it is not clear how a plant will react to an increase in  $\alpha$ -1,4 glucans.

Given the unpredictability of using amylosucrase to produce only  $\alpha$ -1,4 glucans that can be isolated from culture medium, or from a plant for the reasons stated above; given the lack of guidance and examples of using amylosucrase to produce  $\alpha$ -1,4 glucans either in a medium comprising a transformed host cell expressing an amylosucrase enzyme, a transformed plant expressing a heterologous amylosucrase or a solution incubated with amylosucrase and not produce another product that is catalyzed by amylosucrase; and given the state of the art that teaches amylosucrase can catalyze other reactions other than the production of  $\alpha$ -1,4 glucans



Art Unit: 1638

from sucrose and that the enzyme requires specific conditions to produce the  $\alpha$ -1,4 glucans as disclosed by the Applicants, it would require undue experimentation by one skilled in the art to make and/or use the claimed invention.

8. Claims 33-38 and 40-41 are deemed free of the prior art, given the failure of the prior art to teach or reasonably suggest a process for the production of linear  $\alpha$ -1,4 glucans, fructose and/or fructose syrup comprising culturing a host cell and transforming a plant with an expression cassette comprising a nucleic acid molecule encoding an amylosucrase and an in vitro system comprising using an amylosucrase protein producing said compounds.

9. No claims are allowed.

10. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Stuart Baum whose telephone number is (703) 305-6997. The examiner can normally be reached on Monday-Friday 8:30AM – 5:00PM.

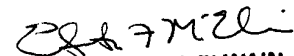
If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Amy Nelson can be reached on (703) 306-3218. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 305-3014 or (703) 305-3014 for regular communications.

Art Unit: 1638

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the legal analyst, Sonya Williams, whose telephone number is (703) 305-2272.

Stuart Baum Ph.D.

October 18, 2002

  
ELIZABETH F. McELWAIN  
PRIMARY EXAMINER  
GROUP 1600